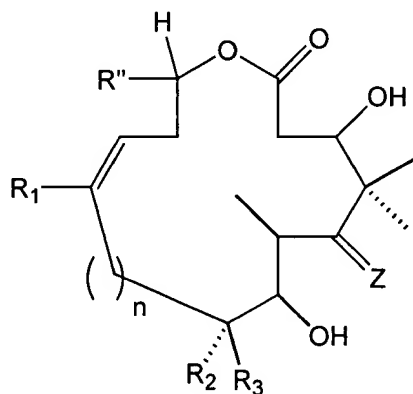


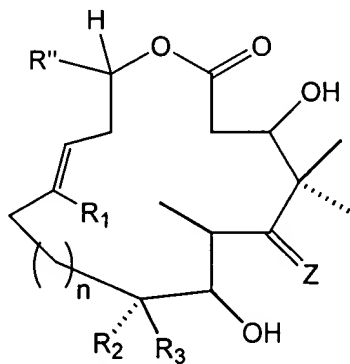
I. Amendment of Claims:

a) Please amend the claims as indicated below. For the convenience of the Examiner, a copy of the complete set of pending claims, in the form that they will take after entrance of the present Amendment, is included herewith at the end of Response.

1. (Amended) A purified compound having the structure:



or a compound having the structure:



[or a pharmaceutically acceptable derivative thereof,]

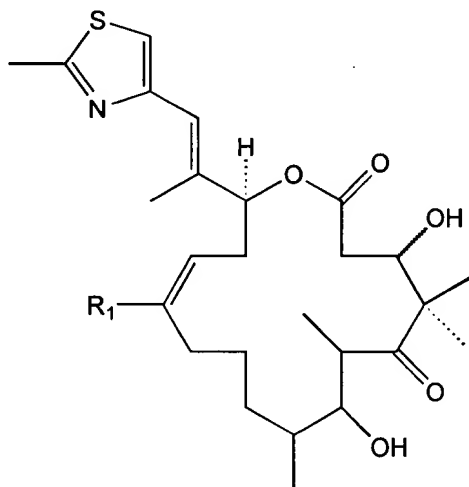
wherein R₁, R₂, and R₃ are each independently H, or linear or branched chain alkyl, [optionally] which alkyl may be singly or multiply substituted by hydroxy, substituted or unsubstituted alkoxy, substituted or unsubstituted carboxy, carboxaldehyde, substituted or unsubstituted, linear or branched alkyl, [or] substituted or unsubstituted cyclic acetal, fluorine, NR₄R₅, N-hydroximino, or N-alkoxyimino, wherein R₄ and R₅ are independently H, phenyl, benzyl, linear or branched chain alkyl;

R" is -CY=CHX, or H, linear or branched chain alkyl, phenyl, or 2-methyl-1,3-thiazol-4-yl, wherein X is H, linear or branched chain alkyl, phenyl, or 2-methyl-1,3-thiazol-4-yl, and Y is H or linear or branched chain alkyl;

Z is O, N(OR₆) or N-NR₇R₈, wherein R₆, R₇ and R₈ are independently H or a linear or branched chain alkyl or alkoxy; and

n is 0, 1, 2, or 3.

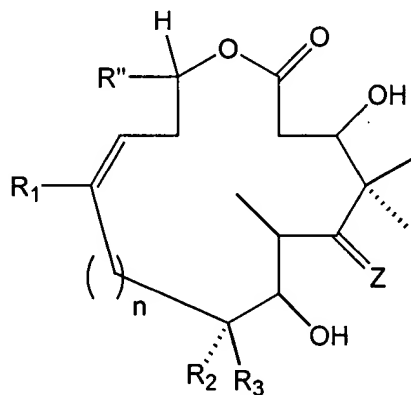
64. (Amended) A purified compound having the structure:



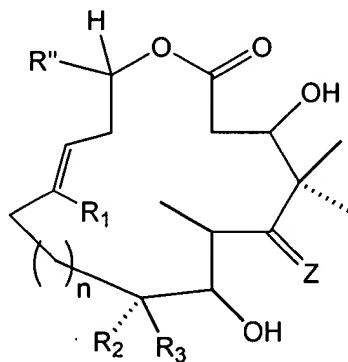
[or a pharmaceutically acceptable derivative thereof,]

wherein R₁ is H, or linear or branched chain alkyl, [optionally] which alkyl may be singly or multiply substituted by hydroxy, substituted or unsubstituted alkoxy, substituted or unsubstituted carboxy, carboxaldehyde, substituted or unsubstituted, linear or branched alkyl, [or] substituted or unsubstituted cyclic acetal, fluorine, NR₄R₅, N-hydroximino, or N-alkoxyimino, wherein R₄ and R₅ are independently H, phenyl, benzyl, linear or branched chain alkyl.

81. (Amended) A pharmaceutical composition comprising:
a compound having the structure:



or a compound having the structure:



[or a pharmaceutically acceptable derivative thereof,]

wherein R₁, R₂, and R₃ are each independently H, or linear or branched chain alkyl, [optionally] which alkyl may be singly or multiply substituted by hydroxy, substituted or unsubstituted alkoxy, substituted or unsubstituted carboxy, carboxaldehyde, substituted or unsubstituted, linear or branched alkyl, [or] substituted or unsubstituted cyclic acetal, fluorine, NR₄R₅, N-hydroximino, or N-alkoxyimino, wherein R₄ and R₅ are independently H, phenyl, benzyl, linear or branched chain alkyl;

R'' is -CY=CHX, or H, linear or branched chain alkyl, phenyl, or 2-methyl-1,3-thiazol-4-yl, wherein X is H, linear or branched chain alkyl, phenyl, or 2-methyl-1,3-thiazol-4-yl, and Y is H or linear or branched chain alkyl;

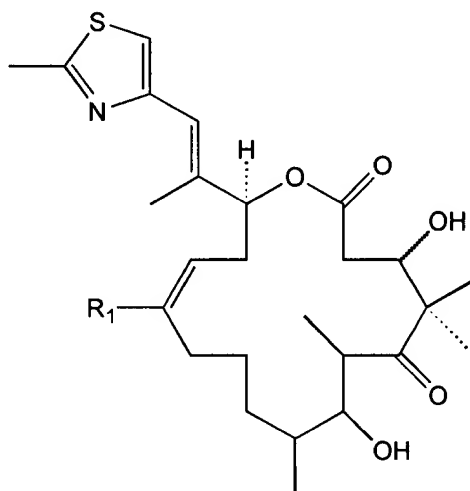
Z is O, N(OR₆) or N-NR₇R₈, wherein R₆, R₇ and R₈ are independently H or a linear or branched chain alkyl or alkoxy; and

n is 0, 1, 2, or 3; and

a pharmaceutically acceptable carrier,

said composition optionally further comprising a cytotoxic agent.

87. (Amended) A pharmaceutical composition comprising:
a compound having the structure:



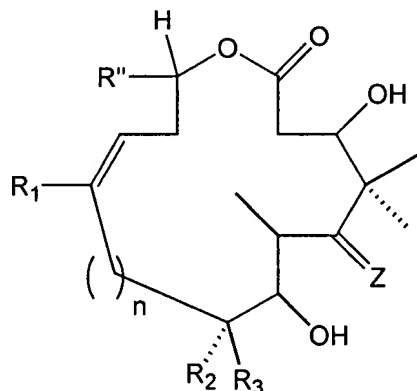
[or a pharmaceutically acceptable derivative thereof,]

wherein R₁ is H, or linear or branched chain alkyl, [optionally] which alkyl may be singly or multiply substituted by hydroxy, substituted or unsubstituted alkoxy, substituted or unsubstituted carboxy, carboxaldehyde, substituted or unsubstituted, linear or branched alkyl, [or] substituted or unsubstituted cyclic acetal, fluorine, NR₄R₅, N-hydroximino, or N-alkoxyimino, wherein R₄ and R₅ are independently H, phenyl, benzyl, linear or branched chain alkyl; and

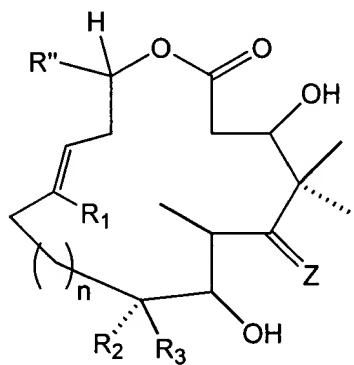
a pharmaceutically acceptable carrier,

said composition optionally further comprising a cytotoxic agent.

110. (Amended) A method of treating cancer in a subject comprising:
 administering to the subject a therapeutically effective amount of a compound having the
 structure:



or a compound having the structure:



[or a pharmaceutically acceptable derivative thereof,]

wherein R_1 , R_2 , and R_3 are each independently H, or linear or branched chain alkyl,
 [optionally] which alkyl may be singly or multiply substituted by hydroxy, substituted or
 unsubstituted alkoxy, substituted or unsubstituted carboxy, carboxaldehyde, substituted or
 unsubstituted, linear or branched alkyl, [or] substituted or unsubstituted cyclic acetal, fluorine,
 NR_4R_5 , N-hydroximino, or N-alkoxyimino, wherein R_4 and R_5 are independently H, phenyl,
 benzyl, linear or branched chain alkyl;

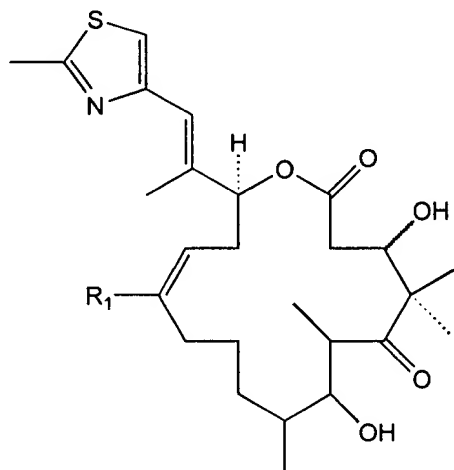
R'' is $-CY=CHX$, or H, linear or branched chain alkyl, phenyl, or 2-methyl-1,3-thiazol-4-
 yl, wherein X is H, linear or branched chain alkyl, phenyl, or 2-methyl-1,3-thiazol-4-yl, and Y is
 H or linear or branched chain alkyl;

Z is O, N(OR₆) or N-NR₇R₈, wherein R₆, R₇ and R₈ are independently H or a linear or branched chain alkyl or alkoxy; and

n is 0, 1, 2, or 3,

said method optionally further comprising administering a cytotoxic agent.

116. (Amended) A method for treating cancer in a subject comprising:
administering to a subject a therapeutically effective amount of a compound having the structure:



[or a pharmaceutically acceptable derivative thereof,]

wherein R₁ is H, or linear or branched chain alkyl, [optionally] which alkyl may be singly or multiply substituted by hydroxy, substituted or unsubstituted alkoxy, substituted or unsubstituted carboxy, carboxaldehyde, substituted or unsubstituted, linear or branched alkyl, [or] substituted or unsubstituted cyclic acetal, fluorine, NR₄R₅, N-hydroximino, or N-alkoxyimino, wherein R₄ and R₅ are independently H, phenyl, benzyl, linear or branched chain alkyl,

said method optionally further comprising administering a cytotoxic agent.

II. Rejection of claims 1 and 59-150 under 35 U.S.C. § 112:

The Examiner has rejected claims 1 and 59-150 under 35 U.S.C. § 112, first and second paragraphs, as containing subject matter which was not described in the specification in such a

way to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention, and as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Examiner has particularly objected to the term “derivative” and states that this term has not been defined in the specification.

Applicant disagrees with the Examiner’s assertion that use of the term “derivative” makes the claims indefinite or doesn’t convey to one of skill in the art that the inventors had possession of the claimed invention at the time of filing. Applicant submits that the term “derivative” did not need to be defined in the specification because the term is commonly used in the pharmaceutical arts and Applicant was using the term as defined in *Dorland’s Medical Dictionary* (27th Ed.), “a chemical substance derived from another substance either directly or by modification or partial substitution.” A derivative would include modified compounds such as pro-drugs, esters, amides, acetylated forms, protected forms, glycosylated forms, and conjugated forms of the claimed epothilone analogs. One of skill in the art would appreciate this meaning of derivative and would understand that these compounds are included within the scope of the present claims. Therefore, the claims are not indefinite nor do they lack written description.

However, in order to further prosecution, Applicant has amended the independent claims to remove the phrase “pharmaceutically acceptable derivative thereof”. Applicant though reserves the right to pursue claims reciting pharmaceutically acceptable derivatives in future continuation or divisional applications. Applicant respectfully submits that the amendment obviates the rejections under 35 U.S.C. § 112 and requests that the rejection be removed.

III. Rejection of claims 1, 59-61, and 63-66 under 35 U.S.C. § 101:

The Examiner has rejected claims 1, 59-61, and 63-66 under 35 U.S.C. § 101 as claiming the same invention as that of claims 1-6 of U.S. Patent 6,242,469. However, Applicant disagrees that claims 1, 59-61, and 63-66 are directed to the same invention as claims 1-6 of U.S. Patent 6,242,469 (the ‘469 patent).

35 U.S.C. § 101 prevents two patents claiming the “same invention” from issuing. The courts have defined “same invention” in the statutory double patenting context as meaning identical subject matter. *In re Vogel* 57 C.C.P.A. 920, 422 F.2d 438 (1970). The court in *In re*

Vogel gave as an example of two inventions that are not the same a claim reciting “halogen” as compared to a claim reciting “chlorine”. The court concluded that the former is broader than the latter and that therefore the two inventions are *not* the same. A test the court offered to be applied in determining “same invention” is whether one could literally infringe one of the claims without literally infringing the other. If one can literally infringe one claim without infringing the other, the claims do not define the same invention. A copy of *In re Vogel* has been included herewith for the Examiner’s convenience.

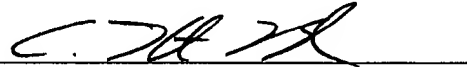
If this “same invention” test is applied to the present application versus the ‘469 patent, it is readily apparent that the claimed inventions are not the same invention because one could imagine a compound which would literally infringe the claims of the present application but would not infringe the claims of the ‘469 patent. Since the claimed inventions are not the same, Applicant submits that the rejection is improper and requests that the rejection be removed.

IV. Rejection of claims 1 and 59-150 under the Judicially Created Doctrine of Obviousness-Type Double Patenting:

The Examiner has rejected claims 1 and 59-150 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over U.S. Patent 6,242,469, U.S. Patent 6,284,781, U.S. Patent 6,369,234, U.S. Patent 6,300,355, patent application U.S.S.N. 09/797,027, and patent application U.S.S.N. 09/796,959. In order to obviate this rejection, Applicant submits herewith Terminal Disclaimers disclaiming the terminal portion of any patent that may issue from the present application over U.S. Patents 6,242,469, 6,284,781, 6,369,234, and 6,300,355, for the purpose of obviating the rejection and progressing toward allowance. Applicant wishes to refrain from addressing the provisional rejections over pending applications until conflicting claims have in fact been allowed.

If it is believed that a telephone conversation would expedite matters, the Examiner is invited to contact the undersigned at (617) 248-5215. The Examiner's attention is also directed to the recent change in power of attorney and correspondence address, as submitted herewith. Although it is believed that there is no fee associated with this amendment, if Applicant is mistaken, please charge any fees to our Deposit Account No.: 03-1721.

Respectfully Submitted,



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Date: April 3, 2003

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I certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner for Patents, Washington, DC 20231.

April 3, 2003
Date

Linda M. Amato
Signature

Linda M. Amato

Typed or Printed Name of person signing certificate